fragments by alcoholic precipitation, said fragments having an increased ratio of anti-Xa titer to USP titer as compared to the starting heparin fragments.

107. The process of claim 101, which comprises recovering the alcoholic-precipitated fragments, subjecting an aqueous solution of said fragments to gel-filtration and recovering the fraction, which fraction has a further increased anti-Xa titer to USP titer ratio.---

REMARKS

Favorable reconsideration of this patent application is respectfully requested. A bona fide and extensive effort has been made to place this application in condition for allowance.

The remembering of the prior claims is noted, but to facilitate examination for the Examiner, a clear copy of all claims is presented.

Applicants herein petition under the provisions of 37 CFR 1.17 for the necessary two extensions of time to February 16, 1984. A check for the necessary fee is attached herewith. The Patent Office furthermore is authorized to debit or credit the account of the undersigned Number 23-0813 for any discrepancy in the amount due.

1. Claims 63-81 were rejected under 35 USC 112, second paragraph, as being "unduly multiplied" and allegedly obscure and concealing the invention. Without giving any reasons, the Examiner has requested that applicants reduce the

number of claims not to exceed 10. Applicants have no intention to obscure or conceal their invention. On the contrary, they intend and do, it is submitted, claim the invention in accordance with 35 USC 112, para. 2, with 37 CFR 1.75(b) and in accordance with M.P.E.P. 706.03(l) "Multiplicity".

In accordance with the M.P.E.P., a number of claims may be selected for examination by the Examiner, but an applicant cannot be limited or restricted in the number of claims which he presents (706.03(b)).

Applicants are also relying on In re Wakefield and Foster, 164 USPQ 637 (CCPA 1970) also cited by the M.P.E.P.

In Wakefield, the Court overruling the Board of Appeals ruled that:

> ~~both unnecessary and confusing~~. We disagree on both points. It is rarely possible to determine necessity for narrower claims at the time of prosecution. An applicant often does not know all the prior art which may be asserted against his broader claims when he litigates his patent. Further, he is never sure that the broader claims will not be successfully attacked on other grounds when litigated in the courts. See, e.g., Graver Tank v. Linde Air Products, 336 U.S. 271, 80 USPQ 451 (1949). Moreover, there is no statutory authority for rejecting claims as being "unnecessary." For these reasons, an applicant should be allowed to determine the necessary number and scope of his claims, provided he pays the required fees and otherwise complies with the statute. This brings us to the board's view that the number of claims was so large as to obscure the invention, thereby failing to comply with the second paragraph of 35 U.S.C. 112. Again we disagree. Each appealed claim is relatively brief and clear in its meaning. Examination of forty claims in a single application may be tedious work, but this is no reason for saying that the invention is obscured by the large number of claims. We note that the claims were clear enough for the examiner to apply references against all of them in his first action. We conclude that the board erred in affirming the multiplicity rejection.

(at page 639) Underscoring supplied.

Also, attention is invited to In re Flint, 162 USPQ 228 (CCPA 1969), Ex parte Promich, 151 USPQ 737 (POBA 1966), and Ex parte King, 144 USPQ 600 (POBA 1964).

However, to advance the prosecution of this application, the claims (in rewritten fresh copy and of simplified format) have been reduced to a total of 26 claims of which 20 are product claims, 2 are therapeutic composition claims, 2 are method of use claims and 2 are method of making the products. This is certainly a reasonable number of claims considering the four statutory subject matters disclosed. Should the Examiner persist in the requirement to restrict to 10 claims, applicants hereby (with respectful protest) elect for examination the following claims: 82, 83, 84, 85, 86, 87, 90, 95, 96 and 102.

Notwithstanding this election and limitation to the 26 claims, applicants retain all rights in the other claims for whatever appropriate purpose may be necessary.

2. The claims were rejected under 35 USC 101 on a "double patenting" rejection for allegedly claiming the same invention as that of the claims of applicants' co-pending application Serial No. 301,611. This rejection is respectfully traversed.

The claims as drawn and presented in this application are distinguishable over those in co-pending application Serial No. 301,611. A comparison of the respective principal claims of both cases will bring this out. It is therefore submitted that the two applications do not claim the same invention. If, and insofar as certain claims do claim the same subject matter, applicants would consider filing a terminal disclaimer.

3. The claims were rejected under 35 USC 112, second paragraph, as being "indefinite" for the reason that there is not sufficient identifying data to adequately define the mucopolysaccharide, such as infrared data and melting point, etc. This rejection is respectfully traversed.

The claims, as presently drawn, define the subject matter which applicants consider their invention, with all the requisite specificity called for under 35 USC 112, para. 2.

The claims specifically call for numerous characteristics which define their "metes and bounds", for instance, structural features solubility data and NMR data, the USP and Yin-Wessler titers (anti-Xa), ratio of these two values and other features. Why would an infrared spectrum be more particular, or the melting point or range, when there is any? The subject matter claimed is adequately in compliance with 35 USC 112, para. 2, especially as the claims are now revised.

4. The Examiner's further rejections of certain claims under 35 USC 112, second paragraph, have been obviated by the newly drawn claims. In particular, the composition claim now calls for a carrier. Alternative terms such as "and/or" have been deleted, and the dependent claims depend on claims which are still in the application.

5. The process claims have been rejected under 35 USC 103 as being unpatentable over the Schmer patent of record. The instant products and process are deemed to be obvious according to the Examiner from the disclosure of said patent since both low and high activity fractions of heparin are set forth in the Schmer patent. This rejection is respectfully traversed.

The Schmer patent discloses a separation process wherein low-activity heparin is separated from high-activity heparin. The specific activity, or anticoagulant potency, of heparin referred to in Schmer is the USP titer and has a value of approximately 150-170 IU/mg (international units/mg) as in commercially available heparin. (See Schmer, column 1, lines 22-27, and this specification, page 6, lines 17-24, page 36, lines 16-17.) The Schmer patent teaches the separation of high- and low-activity heparin into fractions which have activities ranging from approximately 47 IU/mg to 285 IU/mg. (See col. 4, Table I.)

The instant application, however, teaches and claims the preparation of fragments which have low activity as measured by the USP titer, but high activity when measured by the Yin-Wessler titer. A review of the revised process claims, as drawn, will certainly bring this out. As can be observed from the examples on pages 26, 33 and 34, for instance, the mucopolysaccharides of the invention have low USP titers, in the range from about 3.7 to 82, and high Yin-Wessler titers, generally higher than 100, with ratios of Yin-Wessler titers to USP titers generally higher than 6. The mucopolysaccharides with this type of activity profile are capable of inhibiting the Xa factor in a selective manner while having very little effect on overall coagulation. (See the specification page 6, line 25 to page 7, line 4.) There is no suggestion of this type of product or process for making such products in Schmer. For these reasons it is evident that the compounds and process of the instant application are not obvious from the Schmer patent.

6. Finally, the claims had been rejected under 35 USC 103 as being unpatentable over the Lindahl et al ("Lindahl") patent, of record, "which discloses heparin fragments having 14-18 sugar units". The instant compounds and pharmaceutical compositions (the Examiner states) "are deemed to encompass the compounds and compositions of the Lindahl patent or are so closely analogous so as to be obvious therefrom to a person having ordinary skill in the art". The Examiner further states that since "applicants are claiming the same or substantially the same invention as the Lindahl et al patent, the priority documents filed are ineffective to remove said reference". The Examiner calls on applicants to proceed under 37 CFR 1.205, which is the rule setting forth the conditions under which an interference with a patent can be declared.

Applicants' counsel has reviewed the appropriate sections of the Rules and the law. Applicants for reasons submitted below consider that proceeding under 37 CFR 1.205 is not appropriate; rather applicants should be given the benefit of the priority documents, which antedate Lindhal et al.

In effect, the Examiner is calling on applicants to copy the claims of Lindahl et al for purpose of interference. Rule 1.205 (Interference with a Patent; copying claims of a patent) requires that:

> (a) Before an interference will be declared with a patent, the applicant must present in his application, copies of all of the claims of the patent which also define his invention and such claims must be patentable in the application. However, an interference may be declared after copying the claims excluding an immaterial limitation or variation if such immaterial limitation or variation is not clearly supported in the application or if the applicant otherwise makes a satisfactory showing in justification thereof.

It is not seen how claims from the Lindahl et al patent can be made by applicants in the instant application. Lindahl et al claims call for heparin fragments having:

1. 14-18 sugar units,
2. a main component of the disaccharide unit which is L-iduronosyl-2-O-sulphate-N-sulpho-D-glucosamine-6-O-sulphate,
3. unsulphated L-iduronic acid in a position 3-5 sugar units from the unreducing terminal,
4. the unsulphated L-iduronic acid is followed by a unit selected from the group consisting of N-sulpho-D-glucosamine sulphate and N-acetyl-glucosamine in sulphated and unsulphated form.

Claim 2 claims fragments which have equivalent characteristics, expressed in different terms. All other claims explicitly call for these limitations.

What Lindahl et al is disclosing and claiming is a rather specific and special type of 14 to 18 heparin fragments sugar units (see col. 2, lines 19, col. 2, lines 38-59).

The instant application does not disclose heparin fragments of 14-18 sugar units. There is no disclosure of a disaccharide unit as called for by Lindahl et al. Neither is there a disclosure of the unsulphated L-iduronic acid even less, its position, critical features of the Lindahl et al claims. None of these are immaterial

limitations of the Lindahl et al claims. Therefore, in accordance with the rules the claims of the Lindahl et al patent cannot be copied in the instant application.

Applicants also note that an affidavit or declaration under 37 CFR 1.131 is not appropriate in this situation. The instant application Serial No. 204,505, filed November 6, 1980, is a continuation application of application Serial No. 091,164, filed November 5, 1979. Thus, this application benefits already of the date of November 5, 1979, which is prior to the filing date of the Lindahl et al patent, January 4, 1980. Moreover, the instant application is based on and benefits of the priority dates of French patent applications Serial No. 78-31357 filed on November 6, 1978 and Serial No. 79-18873, filed on July 20, 1979. The Lindahl publication (made of record on May 25, 1983) in Proc. Natl. Acad. Sci. was published by the Academy on July 26, 1979 (Exhibit 1. Letter of the Managing Editor). Thus, the instant application antedates the publication date of this publication. Accordingly, the Lindahl et al publication and patent are not prior art applicable to this application and should be accordingly removed.

In view of the above remarks, it is believed that the subject matter claimed is patentable under 35 USC 112, 101 and 103 (Schmer). Favorable action is respectfully requested.

Should the Examiner consider that a telephone discussion with the undersigned would favorably advance the prosectuion of this application or narrow any

outstanding issues, she is respectfully invited to call him at the telephone number indicated below.

Respectfully submitted,

GERARD J. WEISER
Attorney for Applicants
Reg. No. 19,763
Weiser, Stapler & Kimmelman

WEISER, STAPLER & KIMMELMAN
1510 Two Penn Center Plaza
Philadelphia, PA 19102
(215) 563-6600

Exhibit 1: Letter of the Managing Editor
Proceedings, National Academy
of Sciences

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231, on JANUARY 17, 1984

By [signature]
Signature

JANUARY 17, 1984
Date